Introductory Remarks

Claims 1-5 and 7-24 remain pending in this application. Claims 23 and 24 are withdrawn from consideration. Claims 1-5 and 7-24 remain rejected. Claims 1 and 8 are amended herein to make it clearer that the dual phase compositions of the present invention, when mixed at the time of use, emulsify rapidly and uniformly upon vigorous shaking, and demulsify completely within minutes upon resting. The claim amendments are derived from the disclosure in the specification in paragraph 9 on page 3.

Remarks

Claim rejections under 37 CFR §103(a)

1. Claims 1-2, 4-5, 7-9 and 11-22 are rejected under 35 U.S.C. §103(a), allegedly, as being unpatentable over Davis *et al.* (WO 92/09266) in view of Nagy *et al.* (US Patent No. 5,871,758) as evidenced by Sakellariou *et al.* (Colloid Polym. Sci. 1995). More specifically, the Examiner opines that Davis *et al.* (hereinafter "WO'266") discloses the present invention except for the first liquid phase comprising an oil, although it teaches that the first phase is more lipophilic than water. The Examiner relies on the disclosure in Nagy *et al.* (hereinafter "US'758") for this teaching, and avers that the proposed combination is supported by Sakellariou. This rejection is respectfully traversed.

WO'266 discloses a composition for topical application to skin comprising two distinct but miscible phases, at least one of which contains a drug. One of the phases contains water and the other is more lipophilic than the water-containing phase. The two phases are intended to be mixed together on or immediately prior to application. On mixing of the two liquid phases, the resulting mixture is supersaturated with respect to the drug. Highly saturated systems are beneficial, since the rate of drug penetration on topical application will depend largely on the degree of saturation. As discussed on page 3, in lines 29-34 of the reference, the compositions are particularly useful "where use of thin films over long contact times is necessary or advantageous and it is desirable to maintain an enhanced level of percutaneous adsorption for an extended time period". The problem specifically addressed by the reference is the instability of such solutions once applied to the skin, i.e., drug precipitation from the supersaturated solution after topical application. The reference at page 2, lines 26 – 32, acknowledges EP 272 045 for the

disclosure that the incorporation of an anti-nucleating agent into at least one liquid phase of such a supersaturated solution reduces the tendency for drug precipitation.

In the previous office action of November 21, 2008, the Examiner took the position that WO'266 discloses that PVP effects a separation of the phases of the supersaturated solution, opining, concerning the manner of selecting an anti-nucleating agent in the reference, that the language in the reference at page 9, lines 1-8 "...noting which solutions remain clear" meant that the phases separate. The Applicants, in their response to that office action urged that the Examiner misinterpreted "which samples remain clear", and that from a fair reading of the reference, one skilled in the art would appreciate that this language more accurately refers to those samples which remain in the supersaturated or mixed state; that is, where the drug remains supersaturated in the mixture and does not precipitate out, so that there is no phase separation. The Applicants observed that, in contrast to the present invention, in the reference method, PVP does not act as a demixing agent in a dual phase composition, and therefore, that one skilled in the art may conclude from the disclosure in WO'266 that PVP is a stabilizing agent, which is its known function, but not a destabilizing or demixing agent.

The Examiner amends her position in the present office action of November 18, 2009, somewhat, stating "...while the examiner does agree with applicants' statement remain clear does not necessarily mean phase separation, the examiner disagrees with applicants that it necessarily remains in the mixed state. WO'266 teaches that the polyvinyl pyrrolidone would be expected to help maintain the drug in solution. This does not necessarily mean that when two phases with different lipophilicities are mixed that they do not separate out", and the Examiner's further statement that although PVP helps the drug remain in solution rather than precipitate out, this "does not mean that PVP would be interpreted as helping the composition to remain in a mixed state" The Examiner concludes that "...while one of ordinary skill in the art would expect that PVP would help aid in drug solubilization, one of ordinary skill would not necessarily expect the two phases to remain in a mixed state."

Again, the Applicants cannot agree with the Examiner's argument. The Applicants note that the disclosure in WO'266 in the paragraph common to pages 8 and 9, is derived from the disclosure in the paragraph common to pages 2 and 3 of EP 272 045, acknowledged in WO'266, wherein it is stated that "The choice of a suitable anti-nucleating agent...can readily be chosen

by simple experiment. This may be done, for example, by preparing samples of the desired supersaturated drug solution; adding a selection of anti-nucleating agents,...one to each sample; allowing the samples to stand for, say, 2 hours, and noting which samples remain clear, **and thus stable**". This text is essentially identical to the corresponding disclosure in WO'266 (in the paragraph common to pages 8 and 9), with the exception of the bolded text. The bolded text makes it clear that the anti-nucleating agent maintains the integrity of the supersaturated solution (mixed phases) on the skin, thus prolonging the adsorption of the drug from the supersaturated solution into the skin.

Therefore, the only teaching that one skilled in the art could take away from a fair reading of the disclosure in WO'266 is that PVP is useful for stabilizing a two-phase system, even if for a prolonged but limited time. The reference fails to disclose or suggest essential features of the present invention, i.e., the use of a film former, such as PVP, in a demixing-effective amount in a composition which emulsifies rapidly and uniformly upon vigorous shaking, and demulsifies completely upon resting within about 5 to 20 minutes.

Nevertheless, it is the Examiner's position that WO'266 teaches the Applicants' invention except for the more lipophilic phase containing an oil. The disclosure in US'758 is relied on by the Examiner for this teaching, allegedly, since one skilled in the art would be motivated to use oil to solubilize oil soluble actives. However, US'758 does not cure the deficiencies in WO'266, since even if the skilled formulator were motivated to incorporate an oil, as taught in US'758, into the supersaturated solutions in WO'266, the combination would still lack essential features of the present invention; that is, the use of a film former, for example, a non-cationic film former, such as PVP, in a demixing-effective amount in a composition which emulsifies rapidly and uniformly upon vigorous shaking, and demulsifies completely upon resting within about 5 to 20 minutes. For this reason, the present invention as defined in the Applicants' claims is not obvious from the combined teachings in the references.

That the disclosure in Sakellariou, relative to the behavior of PVP, is inconsistent with that disclosure in WO'266 is attributable to the different chemical nature of a colloidal dispersion system, containing particulate matter, as compared with that of an emulsion-type system. In the colloidal system in Sakellariou, phase separation is caused by thermodynamics, i.e., repulsive forces between the PVP and the surfaces of another polymer, i.e., latex particles. The present

compositions are emulsions in which micelles are formed and deformed. No interactions of PVP with a particle surface are involved. In any event, the combination of the disclosures of WO'266 and US'758 with the teaching in Sakellariou cannot support the Examiner's position, since, as discussed above, the anti-nucleating agent, PVP, in the compositions of WO'266, is not taught to demix but to stabilize the mixed phases state of the supersaturated solution.

2. Claims 3 and 10 are rejected under U.S.C. §103(a), allegedly, as being unpatentable over WO'266 in view of US'758 as evidenced by Sakellariou in further view of Smith (US Patent No. 5,658,559; hereinafter US'559). Specifically, the Examiner contends that the present invention is taught by a combination of the disclosures of WO'266, US'758, as evidenced by Sakellariou, except for the specific polyvinylpyrrolidone polymer, polyvinyl pyrrolidone hexadecene. For this teaching, the Examiner relies on US'559, suggesting that one of skill in the art would have been motivated to utilize the copolymer in place of the PVP in the modified compositions taught by the combination of references because, as taught in US'559, this copolymer "prevents evaporation loss of moisture from the skin" and WO'266 teaches that "evaporation determines the duration of the supersaturated state", and because PVP and the copolymer are functional equivalents for the purposes of US'559. This rejection, too, is respectfully traversed.

WO'266, US'758 and Sakellariou are discussed above.

US'559 is concerned with formulating an occlusive or semi-occlusive barrier moisturizing lotion useful for treating pathologies of the skin. The lotion is an oil and water emulsion which includes a barrier polymer, for example, PVP or a copolymer of PVP, such as, polyvinylpyrrolidone/hexadecene copolymer. As the lotion dries on the skin, a polymeric film forms on the surface of the lotion which retains the therapeutic agent in place and in intimate contact with the surface of the skin. The occlusive/semi-occlusive nature of the lotion applied to the skin also prevents water evaporation so that the skin becomes hydrated and facilitates the penetration of the drug contained in the lotion into the skin.

Nevertheless, as the combined teachings in WO'266, US'758 and Sakellariou have not been shown by the Examiner to achieve the Applicants' invention, substituting PVP/hexadecene copolymer for PVP in the modified compositions, since PVP and PVP/hexadecene are disclosed

as equivalents in US'559, still would not cure the deficiencies found the in previous combination. The combined teachings would still be lacking essential features of the Applicants' invention, that is, the use of a film former in a demixing-effective amount in a composition which emulsifies rapidly and uniformly upon vigorous shaking, and demulsifies completely upon resting within about 5 to 20 minutes. Therefore, the Examiner has not established *prima facie* obviousness of the present invention as defined in independent claims 1 and 8. As claims 2-5 and 7, which are appended to claim 1, and as claims 9-22, which are appended to claim 8, include all of the limitations of the respective independent claims, these claims too are patentable over the combination of cited prior art for the same reasons as are claims 1 and 8.

CONCLUSION

The present invention is concerned with a dual phase liquid cosmetic or pharmaceutical composition comprising an aqueous phase and an oil phase in which the oil phase and aqueous phase are present in a ratio of from about 30:70 to about 70:30 by weight of the total composition, and the composition containing a demixing-effective amount of a film forming agent, preferably, a non-cationic film forming agent, wherein the composition emulsifies rapidly and uniformly upon vigorous shaking, and demulsifies completely upon resting within about 5 to 20 minutes.

WO'266 is directed to supersaturated, drug-containing solutions, comprising a mixture of two liquid phases, for topical application to the skin. PVP, present as an anti-nucleating agent in the compositions, functions to stabilize the supersaturated solution (mixed phases) on the skin, thereby minimizing the tendency of the drug to precipitate out, so as to maintain an enhanced level of percutaneous adsorption of the drug for an extended time period.

Incorporating oils into the WO'266 compositions, as taught by US'758 would not be expected to change the nature of the WO'266 compositions, and therefore could not result in the claimed invention as defined in the Applicants' claims which call for a dual phase composition containing a demixing-effective amount of a film forming agent, preferably, a non-cationic film forming agent, wherein the composition emulsifies rapidly and uniformly upon vigorous shaking, and demulsifies completely upon resting within about 5 to 20 minutes.

The teaching in US'559 also would not cure the deficiencies of the modified compositions, since substituting PVP/hexadecene copolymer for the PVP also would not be expected to change the nature of the supersaturated solutions stabilized by PVP.

For these reasons, the present invention, as defined in claims 1 and 8, and the claims appended thereto, is patentable over the cited references. It is respectfully requested that the rejections of record be withdrawn and a notice of allowance issued.

A petition and fee for extension of time for two months are being submitted concurrently with the RCE and this paper.

Respectfully submitted,

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